

In re Application of: Michal DANIELY et al
Serial No.: 10/771,440
Filed: February 5, 2004
Office Action Mailing Date: December 27, 2006

Examiner: Duffy, Bradley
Group Art Unit: 1643
Attorney Docket: 26003

In the Claims:

1. (Withdrawn) A method of identifying cancerous cells in a biological sample comprising:

(a) staining nucleated cells of the biological sample with at least two stains to thereby obtain stained nucleated cells, and;

(b) sequentially and/or simultaneously exposing said stained nucleated cells to at least two imaging modes, to thereby identify the cancerous cells in the biological sample.

2. (Withdrawn) The method of claim 1, wherein each imaging mode of said at least two imaging modes is specific to a stain of said at least two stains.

3. (Withdrawn) The method of claim 1, wherein the cancerous cells are associated with a cancer selected from the group consisting of leukemia, lymphoma, brain cancer, cerebrospinal cancer, bladder cancer, prostate cancer, breast cancer, cervix cancer, uterus cancer, ovarian cancer, kidney cancer, esophagus cancer, lung cancer, colon cancer, pancreatic cancer, and melanoma.

4. (Withdrawn) The method of claim 1, wherein the biological sample is selected from the group consisting of bone marrow cells, lymph nodes cells, peripheral blood, cerebrospinal fluid, urine, effusions, fine needle aspirates, peripheral blood scrapings, paraffin embedded tissues, and frozen sections.

5. (Withdrawn) The method of claim 1, wherein each stain of said at least two stains is independently selected from the group consisting of a

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morphological stain, an immunological stain, an activity stain, a cytogenetical stain, *in situ* hybridization stain and a DNA stain.

6. (Withdrawn) The method of claim 5, wherein said morphological stain is selected from the group consisting of May-Grünwald-Giemsa stain, Giemsa stain, Papanicolau stain, Hematoxylin-Eosin stain and DAPI stain.

7. (Withdrawn) The method of claim 5, wherein said immunological stain is selected from the group consisting of fluorescently labeled immunohistochemistry, radiolabeled immunohistochemistry and immunocytochemistry.

8. (Withdrawn) The method of claim 5, wherein said activity stain is selected from the group consisting of cytochemical stain and substrate binding assay stain.

9. (Withdrawn) The method of claim 5, wherein said cytogenetical stain is selected from the group consisting of G-banding stain, R-banding stain, Q-banding stain, and C-banding stain.

10. (Withdrawn) The method of claim 5, wherein said *in situ* hybridization stain is selected from the group consisting of fluorescent *in situ* hybridization (FISH) stain, radiolabeled *in situ* hybridization stain, Digoxigenin labeled *in situ* hybridization stain and biotinylated *in situ* hybridization stain.

11. (Withdrawn) The method of claim 5, wherein said DNA stain is a DNA-binding fluorescent dye.

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12. (Withdrawn) The method of claim 1, wherein a first stain of said at least two stains is a morphological stain and a second stain of said at least two stains is selected from the group consisting of an immunological stain, an activity stain, an *in situ* hybridization stain, and a DNA stain.

13. (Withdrawn) The method of claim 1, wherein a first stain of said at least two stains is an immunological stain and a second stain of said at least two stains is selected from the group consisting of a morphological stain, an activity stain, an *in situ* hybridization stain, and a DNA stain.

14. (Withdrawn) The method of claim 1, wherein a first stain of said at least two stains is an activity stain and a second stain of said at least two stains is selected from the group consisting of a morphological stain, an immunological stain, an *in situ* hybridization stain, and a DNA stain.

15. (Withdrawn) The method of claim 1, wherein a first stain of said at least two stains is a cytogenetical stain and a second stain of said at least two stains is selected from the group consisting of an immunological stain, an *in situ* hybridization stain, and a DNA stain.

16. (Withdrawn) The method of claim 1, wherein a first stain of said at least two stains is an *in situ* hybridization stain and a second stain of said at least two stains is a DNA stain.

17. (Withdrawn) The method of claim 1, wherein a first stain of said at least two stains is a DNA stain and a second stain of said at least two stains is an *in situ* hybridization stain.

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18. (Withdrawn) The method of claim 1, wherein step (b) is effected using an automated cell imaging device capable of at least dual imaging.

19. (Withdrawn) A method of diagnosing cancer in a subject, the method comprising:

- (a) obtaining a biological sample from the subject;
- (b) staining nucleated cells of said biological sample with at least two stains to thereby obtain stained nucleated cells, and;
- (c) sequentially and/or simultaneously exposing said stained nucleated cells to at least two imaging modes, to thereby determine the presence or absence of cancerous cells within said stained nucleated cells, wherein presence of said cancerous cells is indicative of a positive cancer diagnosis.

20. (Withdrawn) The method of claim 19, wherein each imaging mode of said at least two imaging modes is specific to a stain of said at least two stains.

21. (Withdrawn) The method of claim 19, wherein the cancer is selected from the group consisting of leukemia, lymphoma, brain cancer, cerebrospinal cancer, bladder cancer, prostate cancer, breast cancer, cervix cancer, uterus cancer, ovarian cancer, kidney cancer, esophagus cancer, lung cancer, colon cancer, pancreatic cancer, and melanoma.

22. (Withdrawn) The method of claim 19, wherein said biological sample is selected from the group consisting of bone marrow cells, lymph nodes cells, peripheral blood, cerebrospinal fluid, urine, effusions, fine needle aspirates and/or peripheral blood scrapings, paraffin embedded tissues, and frozen sections.

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23. (Withdrawn) The method of claim 19, wherein each stain of said at least two stains is independently selected from the group consisting of a morphological stain, an immunological stain, an activity stain, a cytogenetical stain, *in situ* hybridization stain and a DNA stain.

24. (Withdrawn) The method of claim 23, wherein said morphological stain is selected from the group consisting of May-Grünwald-Giemsa stain, Giemsa stain, Papanicolau stain, Hematoxylin-Eosin stain and DAPI stain.

25. (Withdrawn) The method of claim 23, wherein said immunological stain is selected from the group consisting of fluorescently labeled immunohistochemistry, radiolabeled immunohistochemistry and immunocytochemistry.

26. (Withdrawn) The method of claim 23, wherein said activity stain is selected from the group consisting of cytochemical stain and substrate binding assay stain.

27. (Withdrawn) The method of claim 23, wherein said cytogenetical stain is selected from the group consisting of G-banding stain, R-banding stain, Q-banding stain, and C-banding stain.

28. (Withdrawn) The method of claim 23, wherein said *in situ* hybridization stain is selected from the group consisting of fluorescent *in situ* hybridization (FISH) stain, radiolabeled *in situ* hybridization stain, Digoxigenin labeled *in situ* hybridization stain and biotinylated *in situ* hybridization stain.

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29. (Withdrawn) The method of claim 23, wherein said DNA stain is a DNA-binding fluorescent dye.

30. (Withdrawn) The method of claim 19, wherein a first stain of said at least two stains is a morphological stain and a second stain of said at least two stains is selected from the group consisting of an immunological stain, an activity stain, an *in situ* hybridization stain, and a DNA stain.

31. (Withdrawn) The method of claim 19, wherein a first stain of said at least two stains is an immunological stain and a second stain of said at least two stains is selected from the group consisting of a morphological stain, an activity stain, an *in situ* hybridization stain, and a DNA stain.

32. (Withdrawn) The method of claim 19, wherein a first stain of said at least two stains is an activity stain and a second stain of said at least two stains is selected from the group consisting of a morphological stain, an immunological stain, an *in situ* hybridization stain, and a DNA stain.

33. (Withdrawn) The method of claim 19, wherein a first stain of said at least two stains is a cytogenetical stain and a second stain of said at least two stains is selected from the group consisting of an immunological stain, an *in situ* hybridization stain, and a DNA stain.

34. (Withdrawn) The method of claim 19, wherein a first stain of said at least two stains is an *in situ* hybridization stain and a second stain of said at least two stains is a DNA stain.

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35. (Withdrawn) The method of claim 19, wherein a first stain of said at least two stains is a DNA stain and a second stain of said at least two stains is an *in situ* hybridization stain.

36. (Withdrawn) The method of claim 19, wherein step (b) is effected using an automated cell imaging device capable of at least dual imaging.

37. (Currently Amended) A method of identifying transitional cell carcinoma cells in a urine sample comprising:

(a) staining nucleated cells of the urine sample ~~with~~ by at least two staining methods to thereby obtain stained nucleated cells,

~~(b) sequentially and/or simultaneously imaging exposing~~ said stained nucleated cells ~~by~~ to at least two imaging modes, wherein one imaging mode of said at least two imaging modes being different from another imaging mode of said at least two imaging modes.

to thereby identify the transitional cell carcinoma cells in the urine sample.

38. (Canceled)

39. (Original) The method of claim 37, wherein the transitional cell carcinoma cells are associated with bladder cancer and/or kidney cancer.

40. (Original) The method of claim 37, wherein the urine sample is obtained via voided urine or catheterization.

41. (Currently Amended) The method of claim 37, wherein each staining method of said at least two ~~stains~~ staining methods is ~~independently~~ selected from the

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group consisting of a morphological staining, an immunological staining, an activity staining, a cytogenetical staining, *in situ* hybridization staining and a DNA staining.

42. (Currently Amended) The method of claim 41, wherein said morphological staining is selected from the group consisting of May-Grünwald-Giemsa-~~stain~~, Giemsa-~~stain~~, Papanicolau-~~stain~~, Hematoxylin-Eosin ~~stain~~ and DAPI ~~stain~~.

43. (Currently Amended) The method of claim 41, wherein said immunological staining is selected from the group consisting of fluorescently labeled immunohistochemistry, radiolabeled immunohistochemistry and immunocytochemistry.

44. (Currently Amended) The method of claim 41, wherein said activity staining is selected from the group consisting of ~~cytochemical-cytochemistry~~stain and substrate binding assay-~~stain~~.

45. (Currently Amended) The method of claim 41, wherein said cytogenetical staining is selected from the group consisting of G-banding-~~stain~~, R-banding-~~stain~~, Q-banding ~~stain~~, and C-banding-~~stain~~.

46. (Currently Amended) The method of claim 41, wherein said *in situ* hybridization ~~stain~~—is selected from the group consisting of fluorescent *in situ* hybridization (FISH)—~~stain~~, radiolabeled *in situ* hybridization—~~stain~~, Digoxigenin labeled *in situ* hybridization—~~stain~~ and biotinylated *in situ* hybridization—~~stain~~.

47. (Currently Amended) The method of claim 41, wherein said DNA staining is a DNA-binding fluorescent dye.

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48. (Currently Amended) The method of claim 37, wherein a ~~first one~~ staining of said at least two staining methods is a morphological staining and whereas a ~~second another~~ staining of said at least two staining methods is selected from the group consisting of an immunological staining, an activity staining, an *in situ* hybridization-~~stain~~, and a DNA staining.

49. (Currently Amended) The method of claim 37, wherein a ~~first one~~ staining of said at least two staining methods is an immunological staining and whereas a ~~second another~~ staining of said at least two staining methods is selected from the group consisting of a morphological staining, an activity staining, an *in situ* hybridization-~~stain~~, and a DNA staining.

50. (Currently Amended) The method of claim 37, wherein a ~~first one~~ staining of said at least two staining methods is an activity staining and whereas a ~~second another~~ staining of said at least two staining methods is selected from the group consisting of a morphological staining, an immunological staining, an *in situ* hybridization-~~stain~~, and a DNA staining.

51. (Currently Amended) The method of claim 37, wherein a ~~first one~~ staining of said at least two staining methods is a cytogenetical staining and whereas a ~~another second~~ staining of said at least two staining methods is selected from the group consisting of an immunological staining, an *in situ* hybridization-~~stain~~, and a DNA staining.

52. (Currently Amended) The method of claim 37, wherein a ~~first one~~ staining of said at least two staining methods is an *in situ* hybridization ~~stain~~ and

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whereas a second-another staining of said at least two staining methods is a DNA staining.

53. (Currently Amended) The method of claim 37, wherein ~~a first one~~ staining of said at least two staining methods is a DNA staining and whereas a second another staining of said at least two staining methods is an *in situ* hybridization-stain.

54. (Original) The method of claim 37, wherein step (b) is effected using an automated cell imaging device capable of at least dual imaging.

55. (Currently Amended) A method of diagnosing bladder cancer in a subject, the method comprising:

- (a) obtaining a urine sample from the subject;
- (b) staining nucleated cells of said urine sample ~~with~~ by at least two staining methods to thereby obtain stained nucleated cells, and;
- (c) ~~sequentially and/or simultaneously~~ imaging exposing said stained nucleated cells ~~to~~ by at least two imaging modes, wherein one imaging mode of said at least two imaging modes being different from another imaging mode of said at least two imaging modes,

to thereby determine the presence or absence of cancerous cells within said stained nucleated cells, wherein presence of said cancerous cells is indicative of a positive cancer diagnosis.

56. (Canceled)

57. (Original) The method of claim 55, wherein the urine sample is obtained via voided urine or catheterization.

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58. (Currently Amended) The method of claim 55, wherein each staining method of said at least two staining methods is ~~independently~~-selected from the group consisting of a morphological staining, an immunological staining, an activity staining, a cytogenetical staining, *in situ* hybridization ~~stain~~ and a DNA staining.

59. (Currently Amended) The method of claim 58, wherein said morphological staining is selected from the group consisting of May-Grünwald-Giemsa-~~stain~~, Giemsa-~~stain~~, Papanicolau-~~stain~~, Hematoxylin-Eosin-~~stain~~ and/or DAPI ~~stain~~.

60. (Currently Amended) The method of claim 58, wherein said immunological staining is selected from the group consisting of fluorescently labeled immunohistochemistry, radiolabeled immunohistochemistry and immunocytochemistry.

61. (Currently Amended) The method of claim 58, wherein said activity staining is selected from the group consisting of ~~cytochemical~~-cytochemistry ~~stain~~ and substrate binding assay-~~stain~~.

62. (Currently Amended) The method of claim 58, wherein said cytogenetical staining is selected from the group consisting of G-banding-~~stain~~, R-banding-~~stain~~, Q-banding-~~stain~~, and C-banding-~~stain~~.

63. (Currently Amended) The method of claim 58, wherein said *in situ* hybridization ~~stain~~ is selected from the group consisting of fluorescent *in situ* hybridization (FISH)-~~stain~~, radiolabeled *in situ* hybridization-~~stain~~, Digoxigenin labeled *in situ* hybridization ~~stain~~ and biotinylated *in situ* hybridization-~~stain~~.

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64. (Currently Amended) The method of claim 58, wherein said DNA staining ~~is~~ uses a DNA-binding fluorescent dye.

65. (Currently Amended) The method of claim 55, wherein ~~a first one~~ staining ~~of~~ said at least two staining methods is a morphological staining and whereas ~~a second another~~ staining ~~of~~ said at least two staining methods is selected from the group consisting of an immunological staining, an activity staining, an *in situ* hybridization-stain, and a DNA staining.

66. (Currently Amended) The method of claim 55, wherein ~~a first one~~ staining ~~of~~ said at least two staining methods is an immunological staining and whereas ~~a second another~~ staining ~~of~~ said at least two staining methods is selected from the group consisting of a morphological staining, an activity staining, an *in situ* hybridization-stain, and a DNA staining.

67. (Currently Amended) The method of claim 55, wherein ~~a first one~~ staining ~~of~~ said at least two staining methods is an activity staining and ~~a~~ whereas ~~second another~~ staining ~~of~~ said at least two staining methods is selected from the group consisting of a morphological staining, an immunological staining, an *in situ* hybridization-stain, and a DNA staining.

68. (Currently Amended) The method of claim 55, wherein ~~a first one~~ staining ~~of~~ said at least two staining methods is a cytogenetical staining and ~~a~~ whereas ~~second another~~ staining ~~of~~ said at least two staining methods is selected from the group consisting of an immunological staining, an *in situ* hybridization-stain, and a DNA staining.

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69. (Currently Amended) The method of claim 55, wherein ~~a first one~~ staining of said at least two staining methods is an *in situ* hybridization ~~stain~~ and ~~whereas a second another staining~~ -of said at least two staining methods is a DNA staining.

70. (Currently Amended) The method of claim 55, wherein ~~a first one~~ staining ~~-of said at least two staining methods~~ is a DNA staining and ~~a whereas second another staining~~ -of said at least two staining methods is an *in situ* hybridization ~~stain~~.

71. (Currently Amended) The method of claim 55, wherein step (b~~c~~) is effected using an automated cell imaging device capable of at least dual imaging.

72. (New) A method of identifying transitional cell carcinoma cells in a urine sample comprising:

(a) staining nucleated cells of the urine sample by one staining method of at least two staining methods to thereby obtain stained nucleated cells by said one staining method, and subsequently

(b) imaging said stained nucleated cells resultant of step (a); and subsequently

(c) staining said stained nucleated cells resultant of step (a) by another staining method of said at least two staining methods to thereby obtain stained nucleated cells by said another staining method; and subsequently

(d) imaging said stained nucleated cells resultant of step (c); and subsequently

(e) simultaneously viewing said stained nucleated cells resultant of steps (a) and (c)

to thereby identify the transitional cell carcinoma cells in the urine sample.

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73. (New) A method of diagnosing bladder cancer in a subject, the method comprising:

- (a) obtaining a urine sample from the subject;
 - (b) staining nucleated cells of said urine sample by one staining method of at least two staining methods to thereby obtain stained nucleated cells by said one staining method, and subsequently
 - (c) imaging said stained nucleated cells resultant of step (b); and subsequently
 - (d) staining said stained nucleated cells resultant of step (b) by another staining method of said at least two staining methods to thereby obtain stained nucleated cells by said another staining method; and subsequently
 - (e) imaging said stained nucleated cells resultant of step (d); and subsequently
 - (e) simultaneously viewing said stained nucleated cells resultant of steps (b) and (d)
- to thereby determine the presence or absence of cancerous cells within said stained nucleated cells, wherein presence of said cancerous cells is indicative of a positive cancer diagnosis.